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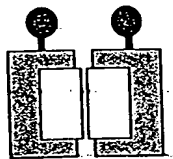
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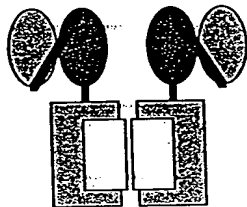
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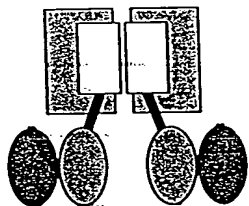
Figure 1



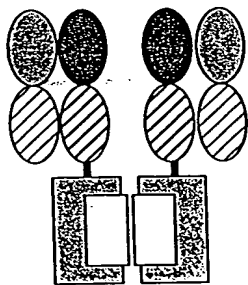
- (A) Small ligand-Caspase Hetero-tetramer (after N-terminal processing)



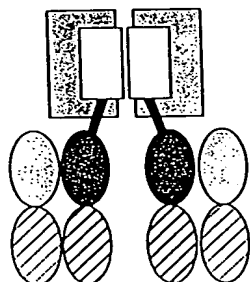
- (B) Single-chain Fv (VL-VH format)-Caspase Hetero-tetramer



- (C) Caspase Hetero-tetramer-Single-chain Fv (VL-VH format)



- (D) Fab-(Heavy chain fusion) Caspase Hetero-tetramer

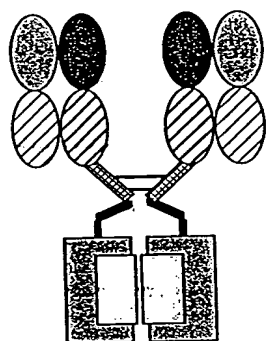


- (E) Caspase Hetero-tetramer Fab-(Heavy chain fusion)

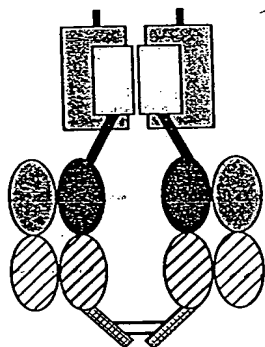
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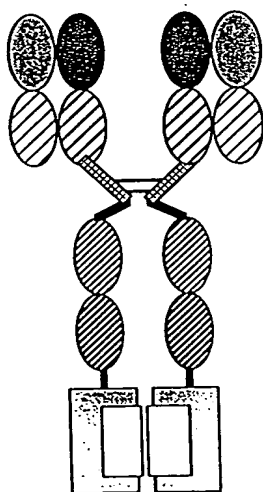
Figure 1 (cont)



(F) F(ab')₂-Caspase heterotetramer
Heavy chain fusion



(G) Caspase heterotetramer-F(ab')₂
Heavy chain fusion



(H) IgG-Caspase heterotetramer

Fig. 1 KEY



VL domain



VH domain



CH1 domain



CL domain



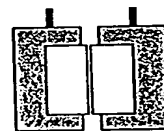
CH2 domain



CH3 domain



small ligand



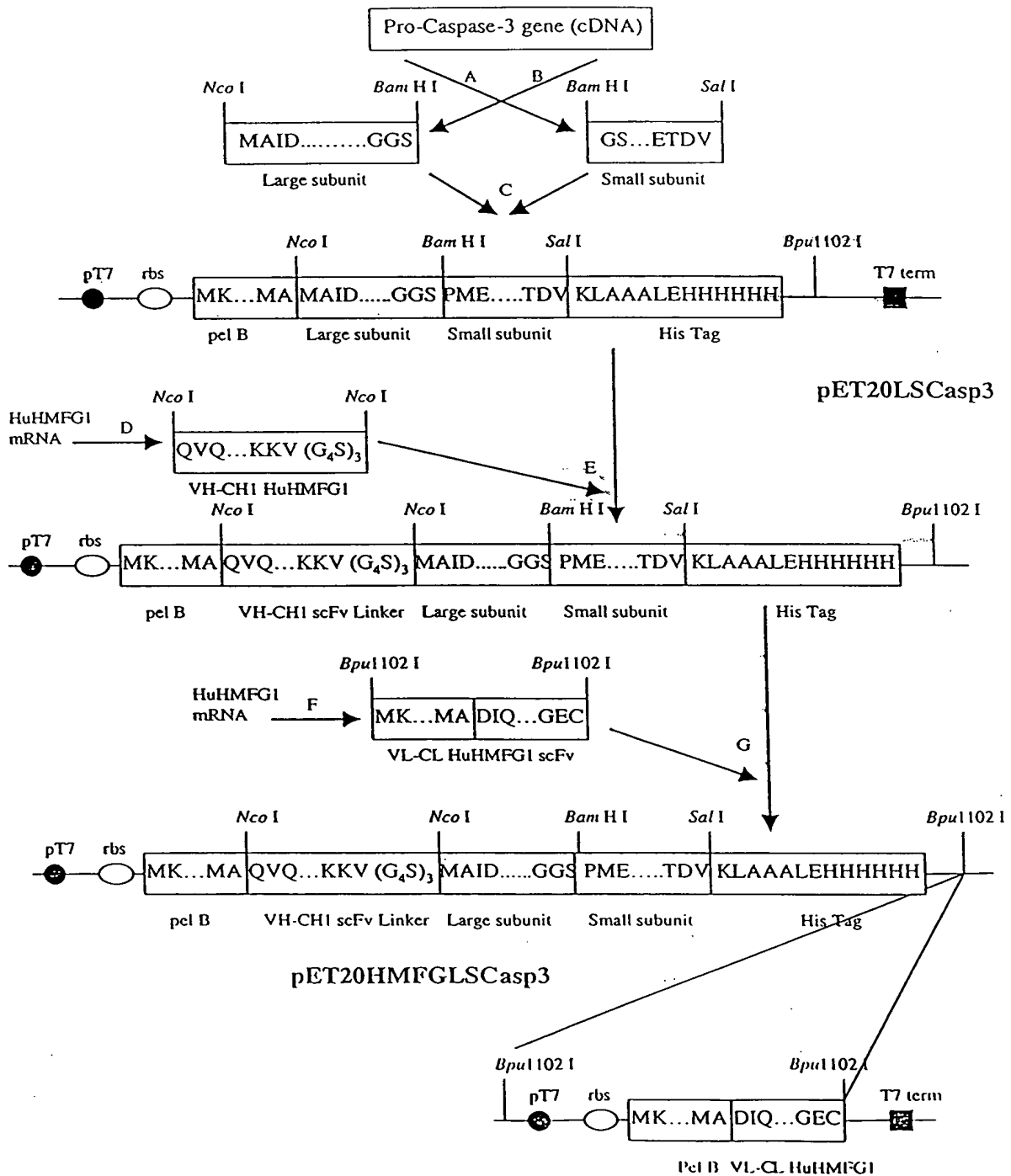
N-term processed
caspase hetero-
tetramer



IgG Hinge

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Figure 2



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Figure 3

1 60
ATGAAATACCTATTGCCTACGGCAGCCGCTGGATTGTTATTACTCGCGGCCAGCCGGCC
M K Y L L P T A A A G L L L L A A Q P A

Nco I

61 120
ATGGCCCAGGTGCAGCTGGTGCAGTCTGGGGCAGAGGTGAAAAAGCCTGGGGCCTCAGTG
M A Q V Q L V Q S G A E V K K P G A S V

121 180
AAGGTGTCCTGCAAGGCTTCTGGCTACACCTTCAGTGCCTACTGGATAGAGTGGGTGCGC
K V S C K A S G Y T F S A Y W I E W V R

181 240
CAGGCTCCAGGAAAGGGCCTCGAGTGGGTCCGAGAGATTTTACCTGGAAGTAATAATTCT
Q A P G K G L E W V G E I L P G S N N S

241 300
AGATACAATGAGAAGTTCAAGGGCCGAGTGACAGTCACTAGAGACACATCCACAAACACA
R Y N E K F K G R V T V T R D T S T N T

301 360
GCCTACATGGAGCTCAGCAGCCTGAGGTCTGAGGACACAGCCGTCTATTACTGTGCAAGA
A Y M E L S S L R S E D T A V Y Y C A R

361 420
TCCTACGACTTTGCCTGGTTTGCTTACTGGGGCCAAGGGACTCTGGTCACAGTCTCCTCA
S Y D F A W F A Y W G Q G T L V T V S S

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Figure 3 (cont)

421 480
GCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGG
A S T K G P S V F P L A P S S K S T S G

481 540
GGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTGCG
G T A A L G C L V K D Y F P E P V T V S

541 600
TGGAACTCAGGCGCCCTGACCAGCGGCGTGACACCTTCCCGGCTGTCCTACAGTCCTCA
W N S G A L T S G V H T F P A V L Q S S

601 660
GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACC
G L Y S L S S V V T V P S S S L G T Q T

661 720
TACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGGTGGGA
Y I C N V N H K P S N T K V D K K V G G

Nco I

721 780
GGCGGTTTCAGGCGGAGGTGGCTCTGGTGGAGGCGGTTCCATGGCGATCGATACAGACAGT
G G S G G G S G G G S M A I D T D S

1261 1320
GGTGTGATGATGACATGGCGTGTGCATAAAATACCAGTGGATGCCGACTTCTTGATGCA
G V D D D M A C H K I P V D A D F L Y A

1321 1380
TACTCCACAGCACCTGGTTATTATTCTTGGCGAAATTCAAAGGATGGCTCCTGGTTTCATC
Y S T A P G Y Y S W R N S K D G S W F I

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Figure 3 (cont)

1381 1440
CAGTCGCTTTGTGCCATGCTGAAACAGTATGCCGACAAGCTTGAATTTATGCACATTCTT
Q S L C A M L K Q Y A D K L E F M H I L

1441 1500
ACCCGGGTTAACCGAAAGGTGGCAACAGAATTTGAGTCCTTTTCCTTTGACGCTACTTTT
T R V N R K V A T E F E S F S F D A T F

1501 1560
CATGCAAAGAAACAGATTCCATGTATTGTTTCCATGCTCACAAAAGAACTCTATTTTTAT
H A K K Q I P C I V S M L T K E L Y F Y

Bam HI

1561 1620
CACGATGAAGTTGATGGTGGATCCCCGATGGAGAACACTGAAAACACTACGTGGATTCAAAA
H D E V D G G S P M E N T E N S V D S K

781 840
TCCATTAAAAATTTGGAACCAAAGATCATAATGGAAGCGAATCAATGGACTCTGGAATA
S I K N L E P K I I H G S E S M D S G I

841 900
TCCCTGGACAACAGTTATAAAATGGATTATCCTGAGATGGGTTTATGTATAATAATTAAT
S L D N S Y K M D Y P E M G L C I I I N

901 960
AATAAGAATTTTCATAAAAGCACTGGAATGACATCTCGGTCTGGTACAGATGTCGATGCA
N K N F H K S T G M T S R S G T D V D A

961 1020
GCAAACCTCAGGGAAACATTTCAGAACTTGAAATATGAAGTCAGGAATAAAATGATCTT
A N L R E T F R N L K Y E V R N K N D L

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Figure 3 (cont)

1021 1080
ACACGTGAAGAAATTGTGGAATTGATGCGTGATGTTTCTAAAGAAGATCACAGCAAAAGG
T R E E I V E L M R D V S K E D H S K R

1081 1140
AGCAGTTTTGTTTGTGTGCTTCTGAGCCATGGTGAAGAAGGAATAATTTTTGGAACAAAT
S S F V C V L L S H G E E G I I F G T N

1141 1200
GGACCTGTTGACCTGAAAAAATAACAACTTTTTTCAGAGGGGATCGTTGTAGAAGTCTA
G P V D L K K I T N F F R G D R C R S L

1201 1260
ACTGGAAAACCCAACTTTTCATTATTCAGGCCTGCCGTGGTACAGAAGTGGACTGTGGC
T G K P K L F I I Q A C R G T E L D C G

Sal I

1261 1320
ATTGAGACACAGGTCGACAAGCTTGCGGCCGCACTCGAGCACCACCACCACCACCCTGA
I E T D V D K L A A A L E H H H H H *

Bpa1102 I

1321 1380
GATCCGGCTGCTAACAAAGCCCGAAAGGGCTGAGTTGGCTGCTGCCACCGCTGAGCGAAA

1381 1440
TTAATACGACTCACTATAGGGAGACCACAACGGTTTCCCTCTAGAAATAATTTGTTTAA

[illegible]

1441 1500
CTTTAAGAAGGAGATATACATATGAAATACCTATTGCCTACGGCAGCCGCTGGATTGTTA
M K Y L L P T A A A G L L

1501 1560
TTACTCGCGGCCAGCCGGCAATGGCCGACATCCAGATGACCCAGAGCCCAAGCAGCCTG
L L A A Q P A M A D I Q M T Q S P S S L

1561 1620
AGCGCCAGCGTGGGTGACAGAGTGACCATCACCTGTAAGTCCAGTCAGAGCCTTTTATAT
S A S V G D R V T I T C K S S Q S L L Y

1621 1680
AGTAGCAATCAAAAGATCTACTTGGCCTGGTACCAGCAGAAGCCAGGTAAGGCTCCAAAG
S S N Q K I Y L A W Y Q Q K P G K A P K

1681 1740
CTGCTGATCTACTGGGCATCCACTAGGGAATCTGGTGTGCCAAGCAGATTTCAGCGGTAGC
L L I Y W A S T R E S G V P S R F S G S

1741 1800
GGTAGCGGTACCGACTTCACCTTCACCATCAGCAGCCTCCAGCCAGAGGACATCGCCACC
G S G T D F T F T I S S L Q P E D I A T

1801 1860
TACTACTGCCAGCAATATTATAGATATCCTCGGACGTTCCGGCCAAGGGACCAAGGTGGAA
Y Y C Q Q Y Y R Y P R T F G Q G T K V E

1861 1920
ATCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTG
I K R T V A A P S V F I F P P S D E Q L

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Figure 3 (cont)

1921 1980
AAATCTGGAAGTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAA
K S G T A S V V C L L N N F Y P R E A K

1981 2040
GTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACACAGAG
V Q W K V D N A L Q S G N S Q E S V T E

2041 2100
CAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGAC
Q D S K D S T Y S L S S T L T L S K A D

2101 2160
TACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTC
Y E K H K V Y A C E V T H Q G L S S P V

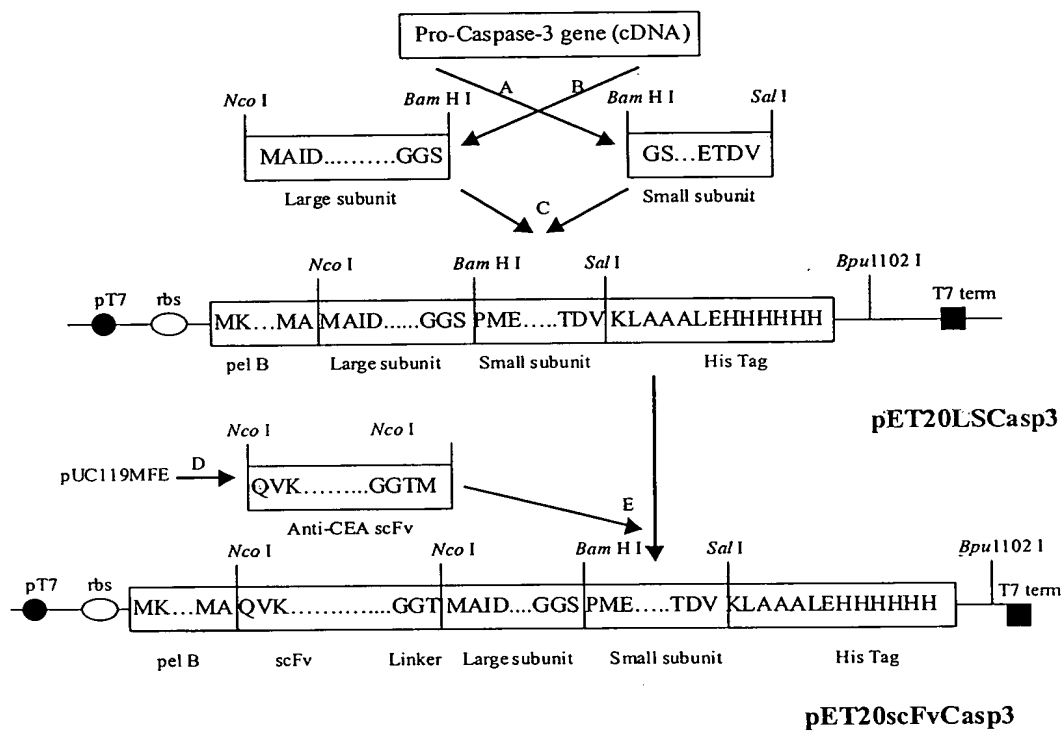
8pu1102 I

2161 2206
ACAAAGAGCTTCAACAGGGGAGAGTGTTAGTAGCAATGGGCTGAGC
T K S F N R G E C * *

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Figure 4



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Figure 5

10 20 30 40 50 60
CCATGGGGCAGGTGAAACTGCAGCAGTCTGGGGCAGAACTTGTGAGGTCAGGGACCTCAG
GGTACCCCGTCCACTTTGACGTCGTCAGACCCCGTCTTGAACACTCCAGTCCCTGGAGTC
M G Q V K L Q Q S G A E L V R S G T S

70 80 90 100 110 120
TCAAGTTGTCCTGCACAGCTTCTGGCTTCAACATTAAAGACTCCTATATGCACTGGTTGA
AGTTCAACAGGACGTGTGCAAGACCGAAGTTGTAATTTCTGAGGATATACGTGACCAACT
V K L S C T A S G F N I K D S Y M H W L

130 140 150 160 170 180
GGCAGGGGCCTGAACAGGGCCTGGAGTGGATTGGATTGATCCTGAGAATGGTGATA
CCGTCCCCGGACTIONTGTCCCGGACCTCACCTAACCTACCTAACTAGGACTCTTACCACTAT
R Q G P E Q G L E W I G W I D P E N G D

190 200 210 220 230 240
CTGAATATGCCCCGAAGTTCCAGGGCAAGGCCACTTTTACTACAGACACATCCTCCAACA
GACTTATACGGGGCTTCAAGGTCCCGTTCCGGTGAAAATGATGTCTGTGTAGGAGGTTGT
T E Y A P K F Q G K A T F T T D T S S N

250 260 270 280 290 300
CAGCCTACCTGCAGCTCAGCAGCCTGACATCTGAGGACACTGCCGTCTATTATTGTAATG
GTCGGATGGACGTGAGTCGTCGGACTGTAGACTCCTGTGACGGCAGATAATAACATTAC
T A Y L Q L S S L T S E D T A V Y Y C N

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Figure 5 (cont)

310 320 330 340 350 360
AGGGGACTCCGACTGGGCGTACTACTTTGACTACTGGGGCCAAGGGACCACGGTCACCG
TCCCCTGAGGCTGACCCGGCATGATGAAACTGATGACCCCGGTTCCCTGGTGCCAGTGGC
E G T P T G P Y Y F D Y W G Q G T T V T

370 380 390 400 410 420
TCTCCTCAGGTGGAGGCGGTTTCAGGCGGAGGTGGCTCTGGCGGTGGCGGATCAGAAAATG
AGAGGAGTCCACCTCCGCCAAGTCCGCCTCCACCGAGACCGCCACCGCCTAGTCTTTTAC
V S S G G G S G G G S G G G S E N

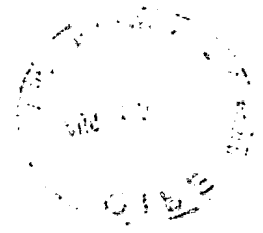
430 440 450 460 470 480
TGCTCACCCAGTCTCCAGCAATCATGTCTGCATCTCCAGGGGAGAAGGTCACCATAACCT
ACGAGTGGGTGAGAGGTCGTTAGTACAGACGTAGAGGTCCCTCTTCCAGTGGTATTGGA
V L T Q S P A I M S A S P G E K V T I T

490 500 510 520 530 540
GCAGTGCCAGCTCAAGTGTAAGTTACATGCACTGGTTCCAGCAGAAGCCAGGCACTTCTC
CGTCACGGTCGAGTTCACATTCAATGTACGTGACCAAGGTCGTCTTCGGTCCGTGAAGAG
C S A S S S V S Y M H W F Q Q K P G T S

550 560 570 580 590 600
CCAAACTCTGGATTTATAGCACATCCAACCTGGCTTCTGGAGTCCCTGCTCGCTTCAGTG
GGTTTGAGACCTAAATATCGTGTAAGTTGGACCGAAGACCTCAGGGACGAGCGAAGTCAC
P K L W I Y S T S N L A S G V P A R F S

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Figure 5 (cont)



610 620 630 640 650 660
GCAGTGGATCTGGGACCTCTTACTCTCTCACAATCAGCCGAATGGAGGCTGAAGATGCTG
CGTCACCTAGACCCTGGAGAATGAGAGAGTGTTAGTCGGCTTACCTCCGACTTCTACGAC
G S G S G T S Y S L T I S R M E A E D A

670 680 690 700 710 720
CCACTTATTACTGCCAGCAAAGGAGTAGTTACCCACTCACGTTCCGGTGCTGGCACCAAGC
GGTGAATAATGACGGTCGTTTCCTCATCAATGGGTGAGTGCAAGCCACGACCGTGGTTTCG
A T Y Y C Q Q R S S Y P L T F G A G T K

730 740 750 760 770 780
TGGAGCTGCAACCGGGAGGTTCTGGAGGAACCATGGCGATCGATACAGACAGTGGTGTG
ACCTEGACGTTGGCCCTCCAAGACCTCCTTGGTACCGCTAGGTATGTCTGTCAACACAAC
L E L Q P G G S G G T M A I D T D S G V

790 800 810 820 830 840
ATGATGACATGGCGTGTCTATAAAATACCAGTGGATGCCGACTTCTTGTATGCATACTCCA
TACTACTGTACCGCACAGTATTTTATGGTCACCTACGGCTGAAGAACATACGTATGAGGT
D D D M A C H K I P V D A D F L Y A Y S

850 860 870 880 890 900
CAGCACCTGGTTATTATTCTTGGCGAAATTCAAAGGATGGCTCCTGGTTCATCCAGTCGC
GTCGTGGACCAATAATAAGAACCGCTTTAAGTTTCCTACCGAGGACCAAGTAGGTCAGCG
T A P G Y Y S W R N S K D G S W F I Q S

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[illegible]

910 920 930 940 950 960
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AAACACGGTACGACTTTGTCATACGGCTGTTCTGAAGCTTAAATACGTGTAAGAATGGGCC
L C A M L K Q Y A D K L E F M H I L T R

970 980 990 1000 1010 1020
TTAACCGAAAGGTGGCAACAGAATTTGAGTCCTTTTCCTTTGACGCTACTTTTCATGCAA
AATTGGCTTTCCACCGTTGTCTTAACTCAGGAAAAGGAACTGCGATGAAAAGTACGTT
V N R K V A T E F E S F S F D A T F H A

1030 1040 1050 1060 1070 1080
AGAAACAGATTCCATGTATTGTTTCCATGCTCACAAAAGAACTCTATTTTTATCACGATG
TCTTTGTCTAAGGTACATAACAAAGGTACGAGTGTTTCTTGAGATAAAAAATAGTGCTAC
K K Q I P C I V S M L T K E L Y F Y H D

1090 1100 1110 1120 1130 1140
AAGTTGATGGTGGATCCCCGATGGAGAACACTGAAAACACTACGTGGATTCAAATCCATTA
TTCAACTACCACCTAGGGGCTACCTCTTGTGACTTTTGATGCACCTAAGTTTTAGGTAAT
E V D G G S P M E N T E N Y V D S K S I

1150 1160 1170 1180 1190 1200
AAAATTTGGAACCAAAGATCATAATGGAAGCGAATCAATGGACTCTGGAATATCCCTGG
TTTTAAACCTTGGTTTCTAGTATGTACCTTCGCTTAGTTACCTGAGACCTTATAGGGACC
K N L E P K I I H G S E S M D S G I S L

[illegible]

1270 1280 1290 1300 1310 1320
ATTTTCATAAAAGCACTGGAATGACATCTCGGTCTGGTACAGATGTTCGATGCAGCAAACC
TAAAAGTATTTTCGTGACCTTACTGTAGAGCCAGACCATGTCTACAGCTACGTCGTTTGG
N F H K S T G M T S R S G T D V D A A N

1330 1340 1350 1360 1370 1380

TCAGGGAAACATTTCAGAACTTGAAATATGAAGTCAGGAATAAAAATGATCTTACACGTG
AGTCCCTTTGTAAGTCTTTGAACTTTATACTTCAGTCCTTATTTTACTAGAAATGTGCAC
L R E T F R N L K Y E V R N K N D L T R

1390 1400 1410 1420 1430 1440

AAGAAATTGTGGAATTGATGCGTGATGTTTCTAAAGAAGATCACAGCAAAAGGAGCAGTT

TTCTTTAACACCTTAACCTACGCACTACAAAGATTTCTTCTAGTGTCGTTTTCTCGTCAA

E E I V E L M R D V S K E D H S K R S S

1450 1460 1470 1480 1490 1500
 TTGTTTGTGTGCTTCTGAGCCATGGTGAAGAAGGAATAATTTTGGAACAAATGGACCTG
 AACAAACACACGAAGACTCGGTACCACTTCTTCCTTATTAAAAACCTTGTTTACCTGGAC
 F V C V L L S H G E E G I I F G T N G P

[illegible]

Figure 6

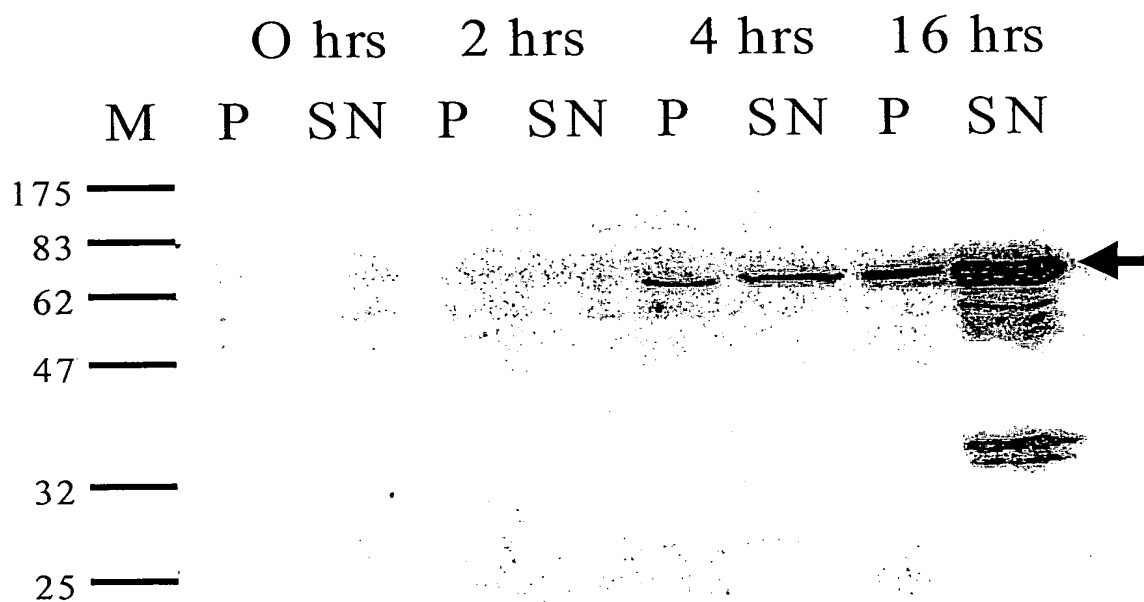
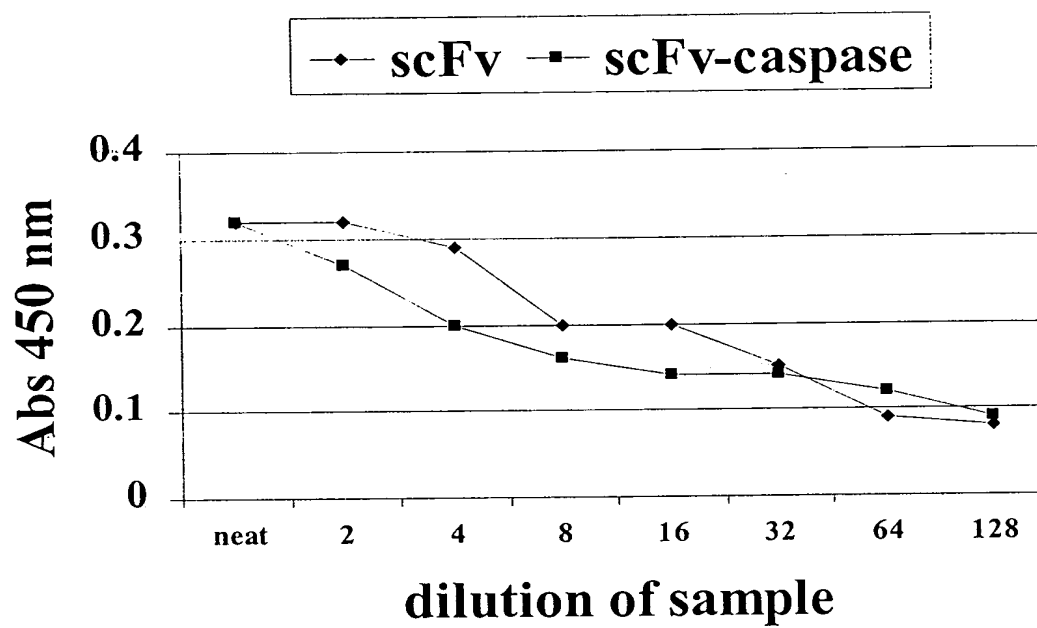


Figure 7



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Figure 8

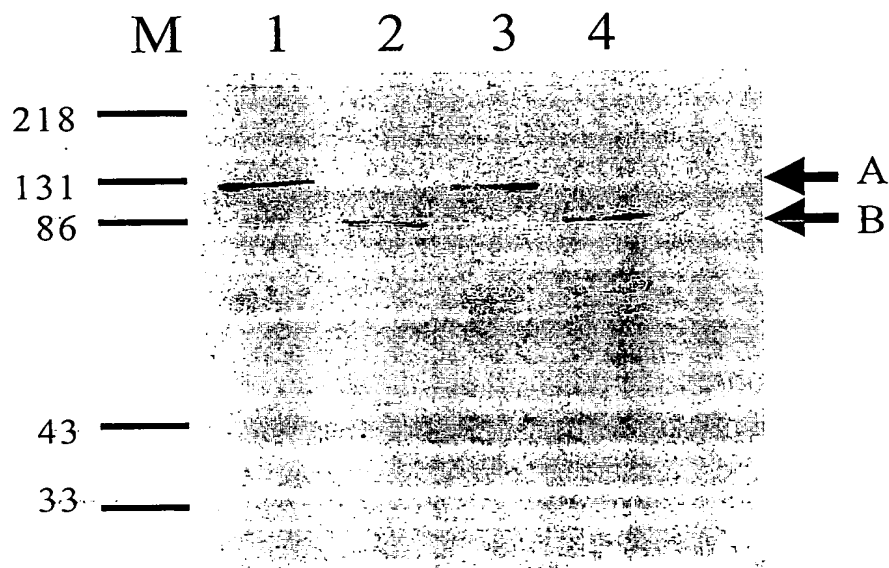
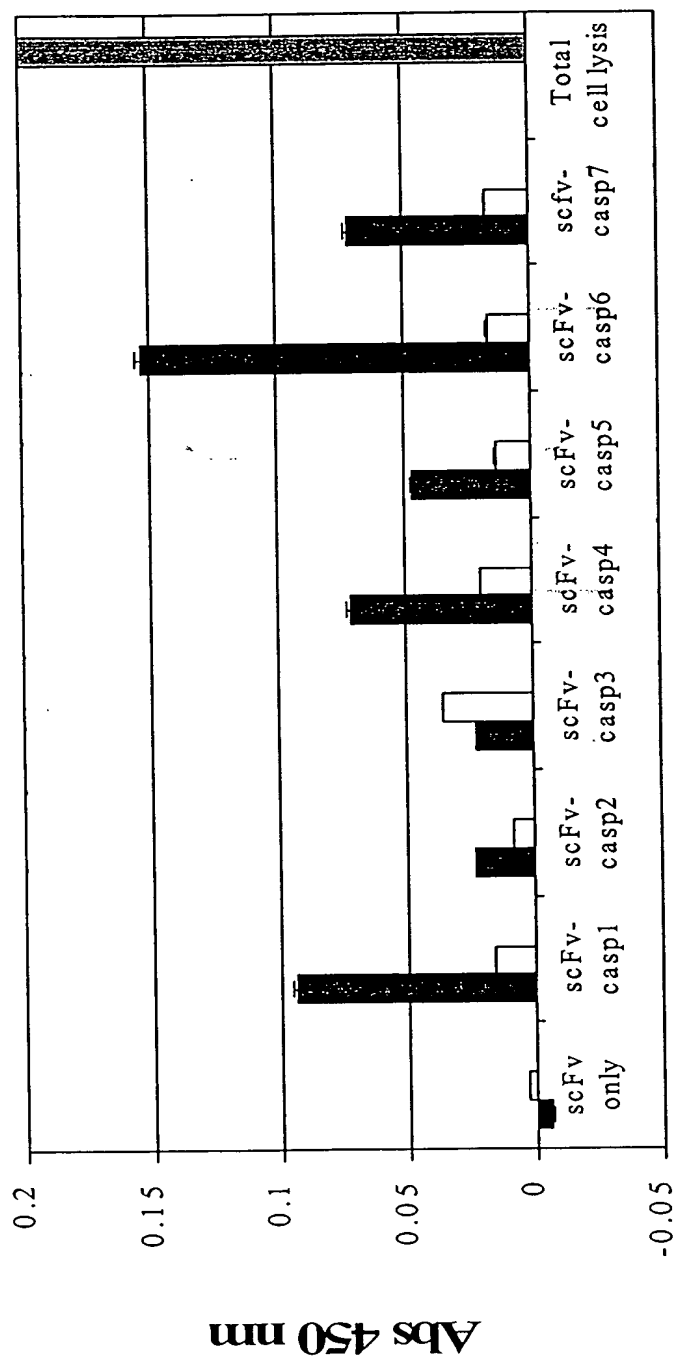


Figure 9



Fusion Protein clones

■ 50 ul □ 10 ul ▨ Total Cell Lysis